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ORIGINAL ARTICLES

DIGITALIS THERAPY: SATISFACTORY EFFECTS IN CARDIAC CASES WITH REGULAR PULSE-RATE.

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In general practice, very commonly the physician fails to get thoroughly satisfactory results from the use of digitalis. As cardiac patients come to the hospital very frequently we find them in a stage of markedly broken compensation though their physician has been prescribing digitalis; and yet in the hospital they respond promptly and effectively to digitalis therapy. Why is this? In part the explanation lies in the fact that under hospital *régime* the patient remains in bed and more completely rests than he is willing to do at home, even though his physician repeatedly has urged upon him the great importance of rest. This more complete rest is an important factor in the patient's improvement, but that it is not the sole factor is shown by observations that I have often made that hospital rest alone does not give the result that is obtained later when it is combined with digitalis therapy.

It seems to me that the chief factor in the failure to get good results from digitalis lies in the improper use of that drug; most commonly the dosage given is insufficient. Insufficient dosage is in part the physician's fault; in part it is due to a poor digitalis preparation furnished by the druggist.

The physician is prone to give quite small doses of digitalis and usually fails to push his dosage to the point of tolerance, as should be done unless a definite effect is produced sooner. How digitalis should be used was tersely stated by William Withering[1] in 1785. "Let the medicine be continued until it either acts on the kidneys, the stomach, the pulse or the bowels; let it be stopped upon the first appearance of any one of these effects." To this might be added, "Until it acts on the respiration." Were this the rule followed today our practitioners would see much better results follow digitalis than they usually do.

It seems that in our books and in our teaching, bad effects from overdosage of digitalis and descriptions of contra-indications to its use have been so emphasized that often the physician actually is afraid to give an adequate dose of digitalis. In a quite extensive hospital experience with cardiac cases I cannot recall a single case admitted from the care of an outside physician in which too much digitalis had been given. Sometimes I have suspected that this was the case from an existent heart-block or from coupling of the beats, or from depression of the T-wave in the electrocardiogram or from nausea and vomiting; but in these cases usually time has shown that heart-block, coupling or depressed T-waves were due to muscle lesions, not to digitalis, and nausea and vomiting were caused by cardiac decompensation, not by digitalis; these patients really needed more digitalis. Per contra, I have seen a great number of cases sent to the hospital really because they were doing poorly on account of the fact that their physician was giving them too little digitalis.

The insufficient dosage of digitalis very frequently is due to the fact that the digitalis preparation is weak; that is, it is far below standard pharmacopeal strength. This has been well emphasized by Pratt[2] in some excellent studies. It seems surprising that poor digitalis is dispensed so frequently when excellent digitalis is grown in many parts of our country, and the testing of the digitalis is reasonably simple.

A great deal of nonsense, in my opinion, is written about digitalis that does not upset the stomach, and much effort appears to be used by our pharmaceutical houses to prepare such forms of digitalis. Most of them do not cause nausea, I suspect, because they are weak forms of digitalis. The fad of fat-free digitalis is an excellent example of this wasted energy. Were this effort directed toward securing a potent active leaf, without which no good digitalis preparation is possible, far better results would obtain. During the past two years I have been using at the Peter Bent Brigham Hospital excellent digitalis grown in Virginia, in Minnesota and in Washington, furnished me by friends. Now the supply of this is exhausted and the leaf furnished by Squibb this month is only half the efficiency of these other leaves, and so preparations made from it will be proportionately inefficient. In passing, I should say that, in my usage of digitalis, preparation plays no part, for I have long since learned that the powdered leaf made freshly into pills is as satisfactory a form of digitalis as either tincture or infusion, and if the leaf is good, just as effective as digipuratum and digifolin, and far less expensive.

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[1] An Account of the Foxglove and Some of its Medical Uses, with Practical Remarks on Dropsy and Other Diseases, Birmingham, 1785.

[2] Boston Med. and Surg. Jour., 1910, clxiii, 279; and Jour. Am. Med. Assn., 1918, lxxi, 618.

Another cause of too small dosage of digitalis lies in the common practice of prescribing tincture of digitalis by drops, and counting a drop as a minim, whereas it generally takes two or three or even more drops to make a minim, as has been emphasized by Pratt[3] and others. Digitalis should be prescribed in weighed or measured amount, not by drops, and enough should be given of a reliable preparation (that means a good leaf as the starting-point of the preparation) to produce a definite effect at least within four days; usually an effect is noted to begin in half this time.

Another reason for not getting good results from digitalis, I think, lies in the very general belief that myocarditis in some way is a contra-indication to digitalis or is a condition in which good therapeutic effects are not to be expected. In my experience in chronic myocarditis, a condition which is a very frequent cause of cardiac failure in people beyond forty, as I have shown in a recent study,[4] most excellent results follow an adequate digitalis therapeusis, and there are no contra-indications to its use, for even in those cases advanced beyond the bound of a therapeutic response no bad effects follow digitalis. In the same way there still lingers the tradition that aortic insufficiency contra-indicates digitalis, because digitalis would prolong diastole and the large regurgitant flow of blood under these conditions would stop the heart in diastolic paralysis; a good enough theory, only it seems to have no basis in fact.

Finally, and this is what I started out to emphasize, very excellent results follow digitalis in hearts that are not fibrillating. Mackenzie, in particular, has so emphasized the value of digitalis in auricular fibrillation that many seem to think if the pulse is regular, digitalis is not liable to give good results, and so it is not pushed in cases with regular rhythm. Pratt[5] says: "My experience with this method has demonstrated that large doses are not dangerous when the cases are carefully followed, and that the drug gives brilliant results in heart failure associated with auricular fibrillation, as Mackenzie has shown, and that it is beneficial in some cases of heart failure with normal rhythm. In hearts with normal rhythm, slowing of the pulse is still generally regarded as a measure of digitalis action, but my observations confirm the findings of Mackenzie[6] and Cohn and Fraser[7] that the drug rarely slows the pulse except in auricular fibrillation until toxic symptoms are produced. . . . It rarely seems to be of benefit in myocardial weakness due to aortic insufficiency, but this valvular lesion is not a contra-indication of its use, as was taught by Corrigan. . . . Rowland, working under Mackenzie, concluded, according to a statement made in the textbook of the latter, that in cases of heart disease with regular rhythm, strophanthin intravenously had very little effect on the general condition and no effect on the pulse-rate or blood-pressure."

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[3] Jour. Am. Med. Assn., 1918, lxxi, 618.

[4] Christian: Jour. Am. Med. Assn., 1918, lxx, 1909.

[5] Ibid., 1918, lxxi, 618.

[6] Heart, 1911, xi, 273.

[7] Tr. XVII International Congress of Medicine, Sec. VI, Medicine, London, 1914.

Of course, it is in the cases with auricular fibrillation that the brilliant results of digitalis are seen most commonly, but I have seen frequently just as good results in chronic cardiac cases with edema in whom there was no irregularity of the pulse or only an occasional extrasystole. The following cases illustrate this very well.

Case I.—P. B. B. H., Med. No. 4963, a man, aged fifty-nine years, was admitted to the hospital on July 10, 1916. Fifteen months before he began to have dyspnea on exertion, and this progressively increased. For thirteen months he had had swollen legs. For twelve months there had been nocturnal dyspnea, severe enough for three months to compel him to sleep sitting in a chair. On admission he had dyspnea, marked subcutaneous edema and ascites. His heart was markedly enlarged, regular in rhythm, and a soft systolic murmur was audible over the precordium. His blood-pressure was: systolic, 220; diastolic, 170. He was considered to be a case of chronic myocarditis and hypertension. At 6 P.M. on July 10 he received 0.1 gm. of powdered digitalis leaves, and this was repeated three times a day until 6 P.M. on July 13, a total of ten doses, or 1 gm. The next day he was begun on 0.05 gm. of powdered digitalis leaves twice a day, and this was continued during his stay in the hospital. The effect of the digitalis therapy is seen in Chart I, where it will be seen that the pulse was not slowed, it being already slow (82), but a striking diuresis and loss of weight occurred (18 kilos, or 39.6 pounds in four days); in the language of Withering, an action on the kidneys.

March 26, 1917, this patient was admitted again with a quite similar condition. Electrocardiograms taken at this time showed left-sided muscular preponderance and a rare auricular extrasystole. From 10 A.M. on March 26 to 12 noon on March 29 he received 0.1 gm. of powdered digitalis leaves four times a day, a total of fourteen doses, or 1.4 gm., and from 6 P.M. on March 29 to 10 P.M. on March 31 a similar dosage twice a day, or a total of 1.8 gm. of digitalis leaves in five days. The result (Chart II) as before was a striking one, with diuresis and a loss in weight of 29.4 kilos, or 64.6 pounds in thirteen days.

June 14, 1917, he was admitted for the third time with a similar prompt diuresis following digitalis, and a loss of weight, 18.8 kilos, or 41.3 pounds in ten days.

September 25, 1917, he came in for the fourth time. A larger amount of digitalis and a longer time were required to produce a diuresis. On September 25 he received digitalis leaves, 0.1 gm. every two hours for five doses. No digitalis was given on September 26 and 27. On September 28 he received four doses of 0.1 gm. at two-hour intervals and then the same does four times a day until 2 P.M. September 30, a total of 1.9 gm. of digitalis since admission. On September 30 diuresis began as shown in Chart III and continued until October 21. From October 1 to 16 he received 0.1 gm.

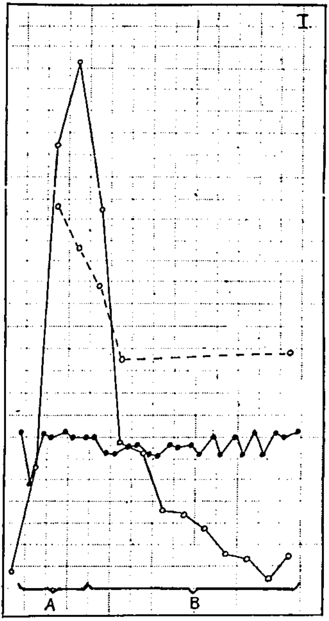

CHART I.—Solid line connecting dots indicates pulse-rate; solid line connecting circles, twenty-four-hour amount of urine in cubic centimeters; broken line connecting circles, weight in kilos; "A," powdered digitalis leaves 0.1 gm. three times a day; "B," powdered digitalis leaves 0.05 gm. twice a day.

digitalis leaves three times a day: in all, forty-six doses, or 6.5 gm. from admission to its discontinuance. During this period his weight decreased 20.2 kilos, or 44.4 pounds. Electrocardiogram at this time showed no arrhythmia.

His fifth admission was on December 3, 1917. Now digitalis produced relatively little effect. By December 26 his auricles had gone into fibrillation, and this persisted. He steadily grew worse and died April 3, 1918. Autopsy showed chronic myocarditis without valve lesion.

In a similar case, that is, one with chronic myocarditis (P. B. B.H., Med. No. 155) admitted June 24, 1913, the effect of strophanthin given intravenously was quite evident, especially on the pulse-rate as shown in Chart IV. One c.c. containing 1 mgm. of strophanthin was given intravenously at 5.10 P.M. on June 25, 3.45 P.M. on July 3 and 11.30 A.M. July 7. The pulse slowed from an average of 120 to 75. This patient had a regular pulse. Diuresis was not so marked in this patient as in the preceding, but he did not have such marked edema.

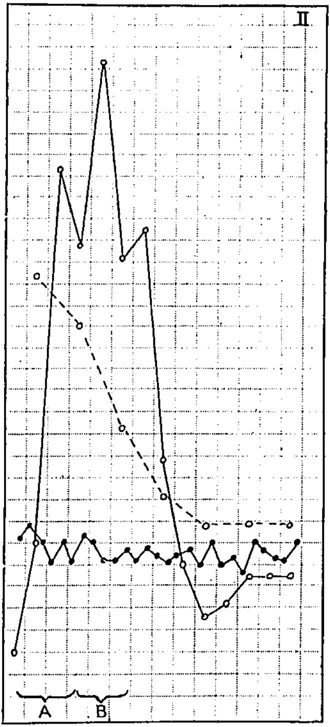

CHART II.—Solid line connecting dots indicates pulse-rate; solid line connecting circles, twenty-four-hour amount of urine in cubic centimeters; broken line connecting circles, weight in kilos; "A," powdered digitalis leaves 0.1 gm. four times a day; "B," powdered digitalis leaves 0.1 gm. twice a day.

His general condition was strikingly improved by the therapeusis. This case is cited, owing to the statement of Rowland, from Pratt's paper. In this case strophanthin intravenously had a

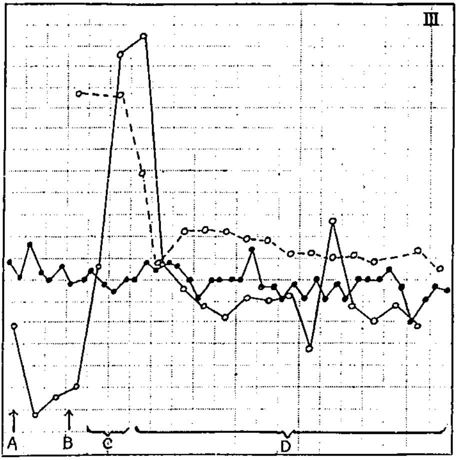

Chart III.—Solid line connecting dots indicates pulse-rate; solid line connecting circles, twenty-four-hour amount of urine in cubic centimeters; broken line connecting circles, weight in kilos; "A," powdered digitalis leaves 0.1 gm. every two hours for five doses; "B," powdered digitalis leaves 0.1 gm. every two hours for four doses; "C," powdered digitalis 0.1 gm. four times a day; "D," powdered digitalis leaves 0.1 gm. three times a day.

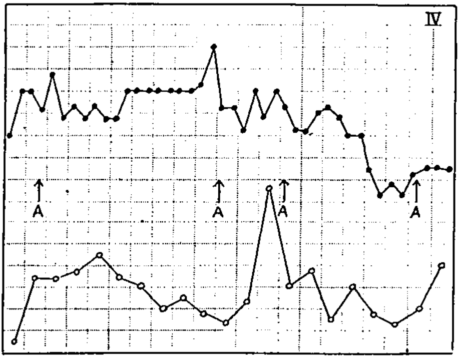

Chart IV.—Solid line connecting dots indicates pulse-rate; solid line connecting circles, twenty-four-hour amount of urine in cubic centimeters; "A," 1 c.c. containing 1 mgm. of amorphous strophanthin intravenously.

very satisfactory effect on both pulse-rate and general condition. The dosage of amorphous strophanthin (Böringer) used was larger than I would at present advise. A 0.5 mgm. repeated once again in the twenty-four hours is safer than a single dose of 1 mgm.

Case II.—Another case (P. B. B. H., Med. No. 2767) shows a good result from digitalis in slowing the pulse-rate (Chart V). This was a man, aged thirty-five years, admitted several times to the hospital. On this admission, May 10, 1915, he was very dyspneic, with Cheyne-Stokes respiration, his heart was enlarged, with a loud blowing systolic murmur heard all over the precordium. His liver was enlarged and pulsating. He had no ascites, no hydrothorax and but little subcutaneous edema. His pulse was alternating but regular in rhythm and electrocardiogram showed only the complex of left-sided muscle preponderance. His condition was considered to be chronic myocarditis. On May 11 he received 1 c.c. of digipuratum intramuscularly and was started on powdered digitalis leaves three times a day. This was continued to May 18, a total of twenty doses, or 2 gm. of the powdered leaf. Besides other changes the pulsus alternans entirely disappeared.

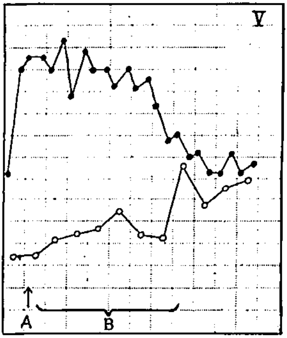

Chart V.—Solid line connecting dots indicates pulse-rate; solid line connecting circles, twenty-four-hour amount of urine in cubic centimeters; "A," 1 c.c. of digipuratum intramuscularly; "B," powdered digitalis leaves 0.1 gm. three times a day.

One more case may be cited.

Case III.—A man, aged thirty-five years (P. B. B. H., Med. No. 6293), was admitted on March 16, 1917, complaining of shortness of breath and swelling of the legs. He had edema, ascites, moderate hydrothorax and a markedly enlarged heart without murmur. He had a pulsus alternans, and electrocardiogram showed distorted ventricular complexes, but no irregularity of rhythm. On the fourth day in the hospital, March 19, he was started on digitalis leaves, 0.1 gm. four times a day, and this was continued until

March 24, a total of nineteen doses, or 1.9 gm. of digitalis leaves. The pulse was moderately decreased in rhythm (Chart VI), a diuresis was produced and his weight decreased in six days 10 kilos or 22 pounds. This patient came again to the hospital on April 6, 1917, for recurrence of his symptoms. On April 6, in the evening, he received 0.2 gm. digitalis leaves and next morning began to receive 0.1 gm. of the same three times a day. This was continued until April 12, or sixteen doses, a total of 1.8 gm. of digitalis leaves, including the first dose of 0.2 gm. This slowed his pulse and produced a diuresis as shown in Chart VII. At each time the patient's general condition was much improved. On a later admission this patient died and autopsy showed an enlarged heart without organic valve lesion, a case of chronic myocarditis.

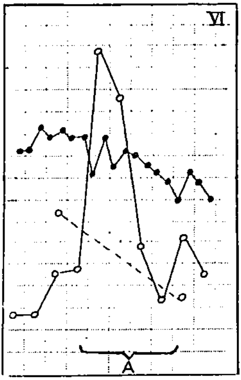

CHART VI.—Solid line connecting dots indicates pulse-rate; solid line connecting circles, twenty-four-hour amount of urine in cubic centimeters; broken line connecting circles, weight in kilos; "A," powdered digitalis leaves 0.1 gm. four times a day.

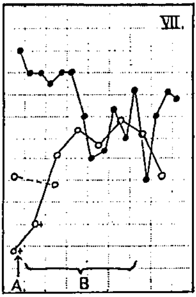

CHART VII.—Solid line connecting dots indicates pulse-rate; solid line connecting circles, twenty-four-hour amount of urine in cubic centimeters; broken line connecting circles weight in kilos; "A," powdered digitalis leaves 0.2 gm.; "B," powdered digitalis leaves 0.1 gm.; three times a day.

In all of these cases there was a striking improvement in the patient's general condition and often a great decrease in dyspnea. The latter frequently is a very striking effect of digitalis in hearts that are regular as well as those that are irregular in rhythm. Such effects, however, cannot be presented graphically.

These cases may serve as examples of what we commonly observe in cardiac cases without arrhythmia, and justify placing much confidence in the effects of digitalis on cardiac patients with regular pulses. They certainly justify a confident use of digitalis in such cases even though the pulse-rate may not be rapid. Even when the pulse-rate is not changed, other striking changes are produced, and the patient is benefited by digitalis therapy when it is properly administered.

A MESOTHELIOMA OF BOTH SUPRARENAL BODIES AND BOTH LUNGS, WITH HEMOTHORAX.

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The uncertain derivation of certain tumors of the upper pole of the kidney and its adnexum, the adrenal, has caused many neoplasms which arise in these organs to be erroneously classed as hypernephromata. Omitting those tumors described by Grawitz[1] as classical of the type hypernephroma, there remain many other distinct varieties of growths to which miscellaneous descriptive names have been applied. Unfortunately, many of these tumors, because of their occurrence in or about the hypernephric region, have been recorded as hypernephromata. Many have received so little description that their identity is lost, and no doubt many of special interest have not been described.

In the present consideration the occurrence of tumors in both adrenals and both lungs, identical in their histopathology and interesting in their cytological picture, together with the interesting clinical picture, form the basis of this report.

A colored male, aged forty-eight years, was brought into the Charity Hospital. He was in a moribund condition and died the following day. There is nothing pertinent in his family history. About five weeks previous to his entrance he noticed "a swelling in the right side of the chest." He had a cough and fever and suffered from shortness of breath. He suffered extreme pain in both sides of the chest, difficulty in breathing and diarrhea.

Physical examination shows an emaciated, anemic negro male, restless, anxious and dyspneic. The respirations are rapid and shallow and chiefly abdominal in type. The right side, while more prominent, is almost stationary during respiration. The supraclavicular regions and Mohreneheim's fossæ are abnormally sunken. The right side from the third rib down anteriorly and laterally, and also posteriorly, shows a marked distention, with bulging of the intercostal spaces. No voice fremitus is felt over the entire right lung, but there is a slight increase on the left side. There is a

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[1] Die sogenannten Lipoma der Niere, Arch. f. path. Anat., etc., Berlin, 1883, xciii, 39.